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EXAMINER
KAM, CHIH MIN

ART UNIT	PAPER NUMBER
1653	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/508,095	Applicant(s) ZUCHT ET AL.	
	Examiner Chih-Min Kam	Art Unit 1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 July 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3 and 6-12* is/are pending in the application.

4a) Of the above claim(s) *3* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Claims

1. Claims 3 and 6-12 are pending.

Applicants' amendment filed July 29, 2002 (Paper No. 18) is acknowledged and applicants' response has been fully considered. Claims 1, 4 and 5 have been cancelled, claim 3 remains withdrawn from consideration, and new claims 6-12 have been added. Thus, claims 6-12 and SEQ ID NO:22 are examined.

2. A newly submitted abstract in Paper N. 18 is acknowledged

Objection Withdrawn

3. The previous objection to the specification regarding the amino acid sequences (at page 3) listed with one letter abbreviation instead of three-letter abbreviation is withdrawn in view of MPEP 2429.

Claim Rejections - 35 USC § 101

4. The previous rejection of claims 1, 4 and 5 under 35 U.S.C.101, regarding the claim recitation of a use without setting forth any steps involved in the process, is withdrawn in view of applicants' cancellation of claims 1, 4 and 5, and applicants' response at page 11 in Paper No. 18.

Claim Rejections - 35 USC § 112

5. The previous rejection of claims 1, 4 and 5 under 35 U.S.C.112, first and second paragraphs, is withdrawn in view of applicants' cancellation of the claim.

Informalities

The disclosure is objected to because of the following informalities:

6. The specification contains amino acid sequences at page 3, but the sequence identifier "SEQ ID NO:" is not given. Each amino acid sequence should be identified with a "SEQ ID NO:". Appropriate correction is required.

7. The specification is objected to for "R_1, R_3 independently represent NH_2" and "R_2, R_4 independently represent COOH, $CONH_2$" (page 3) since each amino acid in the peptide (HN-CH(R)-CO) has already contained the amino (NH) and carbonyl (CO) groups. It is incorrect to write "R_1, R_3 independently represent NH_2" and "R_2, R_4 independently represent COOH, $CONH_2$" for N- and C-terminal ends of the peptide, it should be "R_1, R_3 independently represent H" and "R_2, R_4 independently represent OH, NH_2". Appropriate correction is required.

Claim Objections

8. Claim 7 is objected to for not conforming C.F.R.37 1.822 (d)(1) since the amino acids in the peptide sequences of the invention are listed with one letter abbreviation instead of the required three-letter abbreviation with the first letter as an upper case character. Claim 7 is also objected to for not listing "SEQ ID NO:" for each amino acid sequence.

In response, applicants indicate the three-letter code is only required for Sequence Listing, not for the specification and the claim according to 37 C.F.R. 1.821(a) (2), and the Rule only cover the sequences in which each amino acid is specifically defined as indicated in 37 C.F.R. 1.821(a), while the sequences at page 3 and claim 7 are generic formula. The argument is

not persuasive because the amino acid sequences listed at page 3 and claim 7 contain defined amino acid sequences, thus, each sequence should have a sequence identifier "SEQ ID NO:".

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 6-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for peptides with defined sequences such as SEQ ID NO:17 and SEQ ID NO:19 obtained from cow or human milk via a process of proteolytic cleavage and purification, and having bifidogenic properties; and a method of obtaining these peptides, does not reasonably provide enablement for a peptide obtained from cow or human milk via a process of proteolytic cleavage and purification, or, the derivative or fragment of the peptide, which has bifidogenic property, but the sequence is not defined; and a method of promoting the growth of bifidobacteria or inhibiting the growth of non-bifidobacteria, comprising administering the peptide to an individual. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 6-12 are directed to peptides obtained from cow or human milk via a process of proteolytic cleavage and purification, the derivatives or fragments thereof, which have bifidogenic properties (claims 6-8), a method of obtaining these peptides (claims 9-11), and a method of promoting the growth of bifidobacteria or inhibiting the growth of non-bifidobacteria (claim 12). The specification, however, only discloses cursory conclusions (pages 1-14) without

data supporting the findings, which state that peptides obtained from cow or human milk via a process of proteolytic cleavage and purification, or, their amidated, acetylated, sulfated, phosphorylated, glycosylated or oxidized derivatives or fragments thereof, would have bifidogenic properties (pages 1-2), and some sequences are listed as preferable embodiments (page 3). There are no indicia that the present application enables the full scope in view of peptides obtained from cow or human milk via a process of proteolytic cleavage and purification, and the derivative or fragments thereof as discussed in the stated rejection. The present application provides no indicia and no teaching/guidance as to how the full scope of the claims is enabled. The factors considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d at 731,737, 8 USPQ2d at 1400,1404 (Fed. Cir.1988)). The factors most relevant to this rejection are the breath of the claims, the presence of working examples, the state of the prior art and relative skill of those in the art, the unpredictability of the art, the nature of the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

(1). The breath of the claims:

The breath of the claims is broad and encompasses unspecified variants regarding the derivatives or fragments of the peptides, which are not adequately described or demonstrated in the specification.

(2). The presence or absence of working examples:

The specification only demonstrates certain peptides such as SEQ ID NOs: 17 (casein K-63-117) and 19 (neutrophile lactoferrin 20-67), and the oxidation product exhibit bifidogenic

activity (Example 1, page 8). There are no other working examples indicating the claimed variants or methods in association with the claimed invention.

(3). The state of the prior art and relative skill of those in the art:

Proulx et al. (Lait 74, 139-152 (1994)) indicate the casein hydrolysates produced by three proteolytic enzymes have bifidogenic activity. However, the general knowledge and level of the skill in the art do not supplement the omitted description, the specification needs to provide specific guidance on the identities of the peptide derivatives or fragments, and the treating conditions for promoting the growth of bifidobacteria in individual using the peptide to be considered enabling for variants.

(4). The amount of direction or guidance presented and the quantity of experimentation necessary:

The claims are directed to peptides obtained from cow or human milk via a process of proteolytic cleavage and purification, the derivative or fragments thereof, which have bifidogenic properties, a method of obtaining these peptides, and a method of promoting the growth of bifidobacteria or inhibiting the growth of non-bifidobacteria. The specification indicates the peptides isolated and purified from cow milk or human milk can promote the growth of desired bacteria such as bifidobacteria more than that of other bacteria or by selectively inhibiting the undesired bacteria, which is defined as "bifidogenic" (page 3, first paragraph), and the peptide can be contained in medicaments or in food, and further asserts the peptides are suitable for treating diseases caused by various microorganisms (pages 4-5). The Examples have only indicated the isolation and purification of certain peptides having bifidogenic properties (Example 1, page 8), the method of monitoring the growth-regulating activity on *E. coli*

(Example 2), the method of monitoring the growth-regulating activity on *Bifidobacterium bifidum* (Example 3), and a formula to define bifidogenic activity (Example 4). However, the specification has not identified any derivative or fragment which has the bifidogenic property, and there are no working examples indicating the bifidogenic activities of these derivatives or fragments. Furthermore, there is no *in vitro* or *in vivo* data indicating the peptide, the derivative or fragment is effective in promoting the growth of bifidobacteria or inhibiting the growth of non-bifidobacteria in individual. Therefore, it is necessary to have additional guidance on the identity of the peptide derivatives or fragments, and the treating conditions such as dose for promoting the growth of bifidobacteria in individual, and to carry out further experimentation to assess the effect of the peptides with bifidogenic property.

(5). Predictability or unpredictability of the art:

The claims encompass many peptide variants and the treating conditions such as the dose for various compounds are not described in the specification, the invention is highly unpredictable regarding the outcome of the treatment.

(6). Nature of the Invention

The scope of the claims includes many structural variants, however the specification has not demonstrated the identities and the use of these variants. Thus, the disclosure is not enabling for reasons discussed above.

In summary, the scope of the claim is broad, while the working example does not demonstrate the claimed variants, and the guidance and the teaching in the specification is limited, therefore, it is necessary to have additional guidance and to carry out further experimentation to assess the bifidogenic effect of the claimed invention.

In response, applicants indicate the broad scope of the claim does not indicate the lack of enablement, and the instant disclosure together with the knowledge possessed by one skilled of art provides sufficient information to practice the claimed invention without the exercise of undue experiment. The argument is partially persuasive because the peptides with defined sequence and bifidogenic property are enabled as indicated in the section above, however, the peptides, the derivatives or fragments without identified sequences, and the method of promoting the growth of bifidobacteria in individual are not demonstrated in the specification, thus, they are not enabled.

10. Claims 6-12 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 6-12 are directed to peptides obtained from cow or human milk via a process of proteolytic cleavage and purification, the derivative or fragments thereof, which have bifidogenic properties, a method of obtaining these peptides, and a method of promoting the growth of bifidobacteria or inhibiting the growth of non-bifidobacteria. The specification indicates that peptides obtained from cow or human milk via a process of proteolytic cleavage and purification, or, their amidated, acetylated, sulfated, phosphorylated, glycosylated or oxidized derivatives or fragments thereof, would have bifidogenic properties (pages 1-2), and some sequences are listed as preferable embodiments (page 3). The specification further asserts that SEQ ID NOs: 17 (casein K-63-117) and 19 (neutrophile lactoferrin 20-67), and the oxidation product exhibit bifidogenic activity (Example 1, page 8). However, the specification does not identify the

residues or regions which are modified in various peptide sequences. There is no disclosure indicating the identities of the derivatives or fragments of the peptides which are functional. Without guidance on structure to function/activity, one skilled in the art would not know which region or residue of the peptide is essential for function/activity and how to identify a functional peptide. The lack of a structure to function/activity relationship and the lack of representative species for the derivatives or fragments of the peptides having bifidogenic properties as encompassed by the claims, applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise terms that a skilled artisan would not recognize applicants were in possession of the claimed invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 6-8 and 10-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 6-8 and 10-12 are indefinite because of the use of the term "the derivatives of peptides", "fragments of peptides" or "a fragment thereof". The term "derivatives", "fragments" or "a fragment thereof" renders the claim indefinite, it is unclear what amino acid sequence the peptide has, how different the derivative or fragment is as compared to the parent peptide, and which amino acid is being amidated, acetylated, sulfated, phosphorylated, glycosylated and oxidized. Claims 8 and 10-12 are included in this rejection for being dependent on a rejected claim and not correcting the deficiency of the claim from which they depend.

12. Claim 6 recites the limitation "active substances" in lines 20 and 25. There is insufficient antecedent basis for this limitation in the claim. See also claim 9.

13. Claim 7 is indefinite for using the terms "R_1, R_3 independently represent NH_2" and "R_2, R_4 independently represent COOH, $CONH_2$". It is not clear what groups the N- and C-terminal ends of the peptide have since each amino acid (HN-CH(R)-CO) in the peptide has already contained the amino (NH) and carbonyl (CO) groups. Use of "R_1, R_3 independently represent H" and "R_2, R_4 independently represent OH, NH_2" is suggested. Claim 7 is also indefinite because of the use of "N-modified", it is not clear which site is modified, e.g., is it at N-terminus of the peptide or at the amino side chain of the lysine residue?

14. Claim 6, for example, is indefinite because of the use of the term "combination peptides obtainable by chemical bonding the peptides, ...or oxidized derivatives". The term "combination peptides obtainable by chemical bonding the peptides, ...or oxidized derivatives" renders the claim indefinite, it is unclear what amino acid sequence is obtained as to combining the peptides, fragments or derivatives by chemical bonding. See also claim 10.

15. Claims 7 and 8 are indefinite because the claim contains non-elected sequences.

16. Claim 12 is indefinite because the claim lacks essential steps in the method of promoting the growth of bifidobacteria or inhibiting the growth of non-bifidobacteria. The omitted step is the effective amount of the peptide used and the outcome of the treatment.

In response to various rejections under 35 U.S.C. 112, second paragraph, applicants indicate the claimed language has been changed in the new claims, and the Examiner's definition of a claim limitation cannot conflict with the definition given in the specification (pages 10-11 of the response). The argument is not found persuasive because various terms recited in the claim

are not defined either in the specification or in the claims, thus it is not clear what are the metes and bounds of the terms.

Conclusion

17. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (703) 308-9437. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (703) 308-2923. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-0294 for regular communications and (703) 308-4227 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Chih-Min Kam, Ph. D. CMK
Patent Examiner

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October 5, 2002

Karen Cochrane Carlson PhD

KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER